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PROCAINE AMIDE

[*To the* EDITOR *of the* BRITISH MEDICAL JOURNAL]

SIR,—Since our attention was drawn some time ago by Dr. G. E. H. Enderby to the use of procaine amide to ugment the hypotensive action of hexamethonium, escribed by Dr. A. A. Mason and Dr. J. F. Pelmore *Journal*, January 31, p. 250), we have investigated some f its pharmacological properties. The action of procaine mide has usually been discussed with respect to its direct ardiac action. But, since procaine itself is well known to e able to interfere with ganglionic transmission, a study f the effects of procaine amide on ganglia seemed ecessary.

We have found in cats anaesthetized with chloralose:) that procaine amide in doses of 15 mg./kg. or more ill cause relaxation of the nictitating membrane excited preganglionic stimulation; (2) that in doses of 15 mg./kg. will paralyse the slowing of the heart to vagal stimulaon; (3) that in doses of 15–30 mg./kg. it does not lessen e depressor effect of acetylcholine or the pressor effect adrenaline; (4) in doses of 15 mg./kg. or more it duces the pressor effect of nicotine. In concentration of –50 μg./ml. it reduces the contraction of the guinea-pig's all intestine to nicotine without affecting its response to etylcholine. These observations indicated that procaine ide can interfere with ganglionic function in three nglia at least, the superior cervical ganglion and the gal ganglia of the heart and viscera, without modifying reactions of the effector cells. It remained to determine mechanism of action.

Procaine amide, 10 mg., injected during perfusion of cat's superior cervical ganglion caused complete ure of transmission and abolished release of acetylline on preganglionic nerve stimulation. With the fused ganglion, procaine amide antagonized the nulant effect of acetylcholine on the ganglion. Using electrical recording of ganglion action potentials, caine amide was found to be able to reduce these

considerably without causing any depolarization of the ganglion. These results show that procaine amide has two actions at the ganglion-inhibition of acetylcholine release, and an antagonism to the effects of acetylcholine. The second of these two actions should, of course, simply sum with that of hexamethonium, if the two drugs are given together. But the interaction of the first action, that of preventing acetylcholine release, with the acetylcholine-antagonizing power of hexamethonium, might present novel features. We find, in fact, that in the cat procaine amide and hexamethonium potentiate one another, and that the effect of a mixture is greater than that expected from simple addition of the two components.

It seems probable, therefore, that this synergism between depression of acetylcholine release and competition with acetylcholine could go some way to explain the clinical synergism observed. The question arises whether any of the hypotensive action of procaine amide can be attributed to a direct cardiac action. Our only evidence on this point suggests that, in the cat, this is not true, since the relative potency of procaine amide to hexamethonium in lowering blood pressure is actually less than its relative potency in relaxing the nictitating membrane.

Procaine amide appears to offer, therefore, a new possibility of supplementing the action of a ganglion-blocking agent with a drug active by mouth, with which it might be possible to attack ganglia at present relatively refractory to such agents.—We are, etc.,

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